

REMARKS

The amendments to the specification and claims in the Amendment filed November 15, 2006, were not entered as per the Advisory Action of December 5, 2006. Thus, these amendments are being re-submitted in this Preliminary Amendment. Please note that the amendments to claims 1, 8, 16 and 19 are supported by supported by Figure 2B, the disclosure in paragraph [0028] of the specification, and claim 3 in the Amendment of June 2, 2006.

Claims 4 (which depended from claim 3) and 7 (which depended from claim 4) were objected to as being of improper form for failing to further limit the subject matter of a previous claim. Applicants respectfully traverse this objection.

The Examiner's position is that claim 3 (now canceled and incorporated into independent claims 1, 8 and 16) defines the apparatus of claim 1 as having a polymerase in the chamber. This statement of the Examiner is correct. The Examiner then states that claim 3 further recites an intended use - "which incorporate one or more DNA or RNA precursors." As the phrase "one or more DNA or RNA precursors" was not recited in claim 1 in the Amendment of June 2, 2006, one could be led to believe that the phrase "which incorporate one or more DNA or RNA precursors" refers to an intended use. While this interpretation is not correct, Applicants have clarified any potential confusion by reciting that the "cantilever(s) is [or are] fabricated to respond to deflection and/or resonant frequency shift of the cantilever produced by changes in mass of the attached templates *by addition of at least one complementary mass labeled nucleotide*"<sup>1</sup> in independent claims 1, 8, 16 and 19. At this point, claim 4 has been canceled. Also, claim 7 further limits claim 1. Thus, the objections to claims 4 and 7 should be withdrawn.

Claims 1, 2, 5, 6, 8, 10-18 and 22 were rejected as being anticipated by Baller. This rejection is respectfully traversed and should be withdrawn as independent claims 1, 8 and 16 contain the limitations of claims 3 and 4.

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<sup>1</sup> This limitation is supported by Figure 2B and the disclosure in paragraph [0028] of the specification.

Claims 3, 4, 7 and 19-21 were rejected as being obvious over Baller in view of Melamede. This rejection is respectfully traversed.

Baller fails to disclose the following limitations: “one or more *partially double stranded* nucleic acid templates covalently attached to the at least one cantilever”<sup>2</sup> and “cantilever(s) is [or are] fabricated to respond to deflection and/or resonant frequency shift of the cantilever produced by changes in mass of the attached templates by addition of *at least one* complementary mass labeled nucleotide.” Also, Melamede also fails to fill these gaps. Thus, both Baller and Melamede fail to teach or suggest the claimed invention *as a whole*.

By the embodiments of the present invention it is possible to undertake sequence detection of a nucleic acid template by addition of one complementary nucleotide having a unique mass label at a time to the nucleic acid template as described in paragraph [0028] and Figure 2B of the specification. The sensor system 40 of Baller is simply *not* configured to “respond to deflection and/or resonant frequency shift of the cantilever produced by changes in mass of the attached templates by addition of at least *one* complementary mass labeled nucleotide.” See Figures 4a-4d and corresponding disclosure on pages 12 and 13 of Baller.

The reason why the device of the embodiments of this invention is capable of “respond[ing] to deflection and/or resonant frequency shift of the cantilever produced by changes in mass of the attached templates by addition of at least *one* complementary mass labeled nucleotide” is because the complementary nucleotide could be uniquely labeled with a bulky group, such as nanoparticles and/or nanoparticle aggregates of distinct mass, as disclosed in paragraph [0030] of the specification of the pending application.

Applicants respectfully submit that the Examiner should not read out the limitation “*partially double stranded*” in the limitation “one or more *partially double stranded* nucleic acid templates covalently attached to the at least one cantilever” and the limitation “*at least one*” in the

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<sup>2</sup> *Id.*

limitation “cantilever(s) is [or are] fabricated to respond to deflection and/or resonant frequency shift of the cantilever produced by changes in mass of the attached templates by addition of *at least one* complementary mass labeled nucleotide” of the independent claims just as the Federal Circuit in *Lewmar Marine Inc. v. Bariant Inc.* 827 F.2d 744, 3 USPQ2d 1776, *cert. denied*, 484 U.S. 1007 (Fed. Cir. 1988), explained that even the word “only” cannot be read out of a claim. “The claim limitation could possibly read on the American Eagle winch if the word ‘only’ did not appear in that clause. The word ‘only,’ however, is there and may not be read out of the claims.” *Id.* Similarly, in this case, the word “at least one” and “partially double stranded” may not be read out of the claims.

On page 6 of the Action, the Examiner has acknowledged that Baller fails to disclose addition of a polymerase to the analysis chamber of Baller. Then, the Examiner states that it would have been obvious to add a polymerase to the analysis chamber of Baller based on the disclosure of Melamede. Applicants respectfully submit that this is *not* correct.

Baller only discloses single stranded DNA strands attached to cantilever 41 and reference cantilever 42 to “*detect single stranded* DNA (ssDNA) strand (referred to as target substance) in a reference liquid.” See page 12, lines 2 and 3; also see Figure 4a; emphasis added. However, it is well known to persons of ordinary skill in the art that “[n]o known DNA polymerase is able to begin a new chain (*de novo*). They can only add a nucleotide onto a preexisting 3'-OH group. For this reason, DNA polymerase needs a primer at which it can add the first nucleotide.” See [http://en.wikipedia.org/wiki/DNA\\_polymerase](http://en.wikipedia.org/wiki/DNA_polymerase). In short, Baller does *not* disclose that the cantilever has a *partially double stranded* nucleic acid template (which contains a preexisting 3'-OH group). Instead, Baller discloses that the cantilever has a single stranded nucleic acid template (which does *not* contain a preexisting 3'-OH group). Thus, the addition of a polymerase in the analysis chamber of Baller would simply serve *no* purpose at all. Thus, persons of ordinary skill in the art would not have been motivated to add a polymerase to the analysis chamber of Baller despite the disclosure of Melamede.

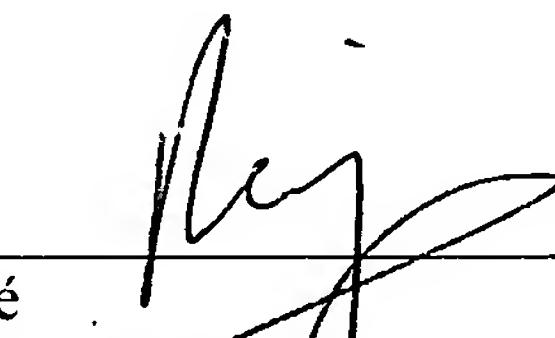
The Examiner further states that one of ordinary skill in the art would have been motivated to add polymerase in the analysis chamber of Baller “for the expected benefit of automated analysis of base sequence during nucleotide addition as desired in the art as taught by Melamede (Column 7, lines 44-46).” See last paragraph on page 6 of the Action. Applicants respectfully submit that the addition of polymerase in the analysis chamber of Baller would *not* likely produce any “expected benefit of automated analysis of base sequence during nucleotide addition” as stated by the Examiner. Applicants respectfully submit that the Examiner has made the above mentioned statement *without* providing any explanation as to how or why the stated benefit would be produced in Baller’s device. Applicants respectfully state that the Examiner owes a better explanation to Applicants (and to the Board if this case goes up on appeal) as to how or why the stated benefit would be produced in Baller’s device as there is no technical or logical reasoning for persons of ordinary skill in this art to believe that the stated benefit could be produced in Baller’s device.

Claims 1-8, 10-22 were provisionally rejected for obviousness type double patenting over claims 15-17, 19-20, 29-30, 34-37 and 42-52 of copending Application No. 10/254,201 in view of Lindsay. As this rejection is a provisional rejection, Applicants are not required to act on it at this time.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **070702009310**.

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